



US006242177B1

(12) **United States Patent**  
**Simmons et al.**(10) **Patent No.: US 6,242,177 B1**  
(45) **Date of Patent: Jun. 5, 2001**(54) **METHODS AND COMPOSITIONS FOR  
SECRETION OF HETEROLOGOUS  
POLYPEPTIDES**(75) Inventors: **Laura C. Simmons**, Burlingame;  
**Daniel G. Yansura**, Pacifica, both of  
CA (US)(73) Assignee: **Genentech, Inc.**, South San Francisco,  
CA (US)(\*) Notice: Subject to any disclaimer, the term of this  
patent is extended or adjusted under 35  
U.S.C. 154(b) by 0 days.(21) Appl. No.: **08/397,303**(22) Filed: **Mar. 1, 1995**(51) **Int. Cl.<sup>7</sup>** ..... **C12Q 1/68**; C07H 21/04;  
C12P 21/02; C12N 15/67(52) **U.S. Cl.** ..... **435/6**; 435/69.1; 435/172.3;  
536/23.7; 536/24.1(58) **Field of Search** ..... 435/6, 69.1, 172.3;  
536/24.1, 23.7(56) **References Cited****U.S. PATENT DOCUMENTS**4,963,495 10/1990 Chang et al. .... 435/320.1  
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262(21):10189-10194 (Jul. 25, 1987).*Primary Examiner*—Nancy Degen(74) *Attorney, Agent, or Firm*—Janet Hasak; Flehr  
Hobach Test Albritton & Herbert LLP(57) **ABSTRACT**

The instant invention discloses the unexpected result that mutant signal sequences with reduced translational strength provided essentially complete processing and high levels of expression of a polypeptide of interest as compared to wild type signal sequences, and that many mammalian polypeptides require a narrow range of translation levels to achieve maximum secretion. A set of signal sequence vectors provides a range of translational strengths for optimizing expression of a polypeptide of interest.

**4 Claims, 21 Drawing Sheets**